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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
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UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NUMBERS 75-51-0243-82 thru 75-51-0245-82
NOVEMBER 1979 - JANUARY 1982

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

AI3-38011	Guinea Pig Sensitization
AI3-38012	Skin Irritation
AI3-38013	Eye Irritation
Photo-irritation	Topical Hazard Evaluation Program
ALD	USDA Proprietary Chemicals

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Preliminary hazard evaluations of candidate insect repellents AI3-38011, -38012, and -38013 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. Chemicals AI3-38011, and 38013 were nonirritating to the skin while -38012 produced mild primary irritation of the skin of rabbits. All chemicals produced mild injury to the cornea, and in addition some injury to the conjunctiva of rabbits. The chemical did not cause photo-irritation or prove to be skin sensitizers or acutely toxic by ingestion. It was recommended that all chemicals be approved for further testing as candidate insect repellents.

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ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Topper/lh/AUTOVON
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REPLY TO ATTENTION OF
HSHB-LT-T/WP

23 APR 1982

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents, US Department of Agriculture Proprietary Chemicals, Study Numbers 75-51-0243-82 thru 75-51-0245-82, November 1979 - January 1982

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

Preliminary hazard evaluations of candidate insect repellents AI3-38011, -38012, and -38013 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. Chemicals AI3-38011 and -38013 were nonirritating to the skin, while -38012 produced mild primary irritation to the skin of rabbits. All chemicals produced mild injury to the cornea, and in addition, some injury to the conjunctiva of rabbits. The chemicals did not cause photo-irritation or prove to be skin sensitizers or acutely toxic by ingestion. It was recommended that all chemicals be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

JOHN F. MAZUR
LTC, MSC
Director, Laboratory Services

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as (5 cy)

CF:
HQDA (DASG-PSP) wo incl
Cdr, HSC (HSPA-P)
Dir, Advisory Cen on Tox, NRC
Comdt, AHS (HSHA-IPM)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO ATTENTION OF
HSHB-LT/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS STUDY NUMBERS 75-51-0243-82 thru 75-51-0245-82 NOVEMBER 1979 - JANUARY 1982

1. AUTHORITY.

a. Letter, US Department of Agriculture, Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, FL, 23 November 1979.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administration; titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Standing Operating Procedures, US Army Environmental Hygiene Agency (USAEHA), 1981.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38011, -38012, and -38013.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate repellents AI3-38011, -38012, and -38013 were conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study, and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*†

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 80-23, revised 1978.
† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemicals AI3-38011 and AI3-38012 did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
0.5 mL technical grade chemical applied to each of six rabbits.	Chemical AI3-38012 caused mild primary irritation of the intact skin and the skin surrounding an abrasion.	USAEHA Category II (ref Appendix A)
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of six New Zealand White rabbits.	All tested chemicals produced mild injury to the cornea, and in addition, some injury to the conjunctiva.	USAEHA Category C (ref Appendix A)
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (male) - no diluent	AI3-38011 = 9700 mg/Kg AI3-38012 = 9700 mg/Kg AI3-38013 = 9700 mg/Kg	All chemicals are relatively nontoxic from accidental ingestion.

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Test	Results	Interpretation
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single 0.05 mL application of a 25 percent (w/v) solution of each chemical and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	A 25-percent solution of each tested chemical in ethanol did not cause a photochemical irritation reaction under test conditions.	All tested chemicals did not cause a photochemical irritation reaction under test conditions and are not expected to cause a photochemical irritation in humans.
Control		
Following UV exposures of the rabbits, 0.05 mL of test chemical, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.	Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	

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Test	Results	Interpretation
SENSITIZATION STUDIES		
Guinea Pigs (Male)		
Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of the tested chemicals or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs for each chemical were given ten sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of each test compound.	Challenge doses of the tested chemicals did not produce a sensitization reaction.	The tested chemicals did not produce sensitization reactions under test conditions and are not expected to produce sensitization reactions in man.
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

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5. CONCLUSION. Technical grade chemicals AI3-38011 and -38013 were nonirritating to the skin while -38012 produced mild primary skin irritation. All tested chemicals produced mild injury to the cornea, and in addition, some injury to the conjunctiva. The chemicals did not cause photo-irritation or prove to be skin sensitizers or acutely toxic by ingestion.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-38011, -38012, and -38013 be approved for further testing as candidate insect repellents.

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Laboratory Animal Veterinary Officer
Toxicology Division

APPROVED:

ARTHUR H. McCREESH, Ph.D.
Chief, Toxicology Division

APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

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APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to this study:

a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

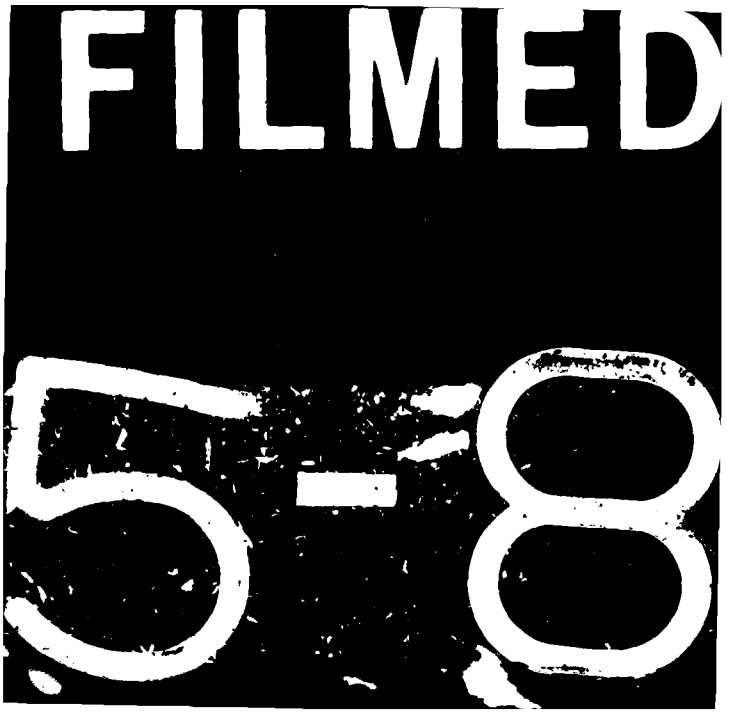
(2) Title 21, Code of Federal Regulations, 1981 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratories Studies.

b. Facilities were inspected during its operational phase to insure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.

Paul V. Sneeringer

PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office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